REMARKS

Claims 1-8, 11, 14, 17, 20-22, 27, 34 and 36 are pending. Claims 5 and 6 have been withdrawn from consideration. Claims 1, 2, 8, 11 and 27 are currently amended.

Support of amendments to claims 1 and 27 can be found throughout the specification disclosure, e.g., at page 2, lines 5-25.

Support for the amendment to claim 2 can be found, e.g., at page 5, lines 1-3.

Support for the amendment to claims 8 and 11 can be found, e.g., at page 5, lines 25-26.

Reconsideration of the application is requested.

§ 112 Rejections

Claims 1-4, 7, 8, 11, 14, 17, 20-22, 27, 34 and 36 stand rejected under 35 USC § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

Claims 1 and 27 have been amended in an effort to address the issues raised in the Office Action. It is submitted that it is clear that the irritation referred to in the claims is irritation of the mucosal tissue caused by the IRM compound, which it is believed would be understood by one of ordinary skill in the art.

With regard to "intermittently applying", the claims do require multiple applications, where at least 50% of the IRM compound applied to the mucosal surface is then intentionally removed from the mucosal surface. This could be using the same or a different applicator (if an applicator is used at all), since the IRM compound being removed is the IRM compound that has be applied to the mucosal surface (i.e., not IRM compound that was just leftover in an applicator). Applicants have also clarified that the language "the IRM that was originally applied" refers to the IRM applied in given intermittent application.

With regard to claim 2, applicants have provided an antecedent basis for "the same device".

With regard to claims 8 and 11, they have been amended to require that the "at least 50%" of the IRM is removed in the specified time periods.

Also, if understood correctly, the Examiner questions on page 5, first paragraph, how a therapeutically effective amount could be achieved even if 100% of the IRM compound can be

removed. The answer is that the IRM compound has already been present for a sufficient amount of time to "jump start" the immune system. This is an important aspect of the invention discussed below.

In summary, Applicants submit that the rejection under 35 USC § 112, second paragraph, has been overcome, and that the rejection should be withdrawn.

Claims 1-4, 7, 8, 11, 14, 17, 20-22, 27, 34 and 36 stand rejected under 35 U.S.C. 112, first paragraph, as allegedly lacking enablement for certain delivery devices such as a suppository. Applicants respectfully traverse.

The specification is clear that there are any number of ways, including those listed by the Examiner, for removing IRM compound from the mucosal surface. For example, while it is preferred to remove the IRM using the same device used for delivery, douching is an alternative. Thus, a suppository could be used to delivery the IRM compound and, if the suppository dissolves or disperses to achieve delivery, a douche could be used for washing off the IRM compound after sufficient time has elapsed to achieve the desired immune response. See page 5, line 3, referencing "douching" as a non-preferred alternative, and page 30, example 10, referencing washing.

In summary, Applicants submit that the rejection under 35 USC § 112, first paragraph, has been overcome, and that the rejection should be withdrawn.

§ 103 Rejections

Claims 1-4, 7, 8, 11, 14, 17, 20-22, 27, 34 and 36 stand rejected under 35 USC § 103(a) as being unpatentable over US 2002/0058674 in view of WO 99/29693 in further view of US patent 6,328,991. Applicants respectfully traverse.

The claimed invention is based in part on the discovery that 1) IRM compounds can be used to "jump-start" the immune response, but do not have to remain present in order to continue the enhanced immune effect, and 2) that removing the IRM compounds after such jump-starting reduces unwanted irritation while remaining effective. Reducing side-effects while maintaining efficacy is extremely important for any drug. As summarized in the specification:

> Although the beneficial effects of IRMs are known, the ability to provide therapeutic benefits via the topical application of an IRM compound to mucosal surfaces for the treatment of mucosal associated conditions is hindered. This is because of the resultant irritation of the mucosal surface that develops with extended contact with an IRM compound and because of undesired systemic delivery of the topically applied IRM compound.
>
> It has now surprisingly been found that the intermittent application of an IRM to a mucosal surface provides a therapeutic benefit without the irritation of the mucosal tissue associated with continuous (or extended) contact with the IRM. Thus, the present invention provides new methods for using IRM compounds to treat or prevent conditions associated with a mucosal surface. In some embodiments, the invention provides methods that are particularly advantageous for the topical application of an IRM to the cervix for treatment of cervical conditions such as cervical dysplasias including dysplasia associated with human papillomavirus (HPV), low-grade squamous intraepithelial lesions, high-grade squamous intraepithelial lesions, atypical squamous cells of undetermined significance (typically, with the presence of high-risk HPV), and cervical intraepithelial neoplasia (CIN).
>
> The present invention provides methods of reducing the irritation of a mucosal surface associated with treating a mucosal associated condition with an IRM. Alternatively stated, the present invention provides methods of delivering an IRM to a mucosal surface so as to achieve immunomodulation with reduced irritation.

None of the cited references discloses that IRM compounds provide continued immune enhancement even after removal from contact, or that irritation can be reduced when this is done.

It is important to note that just because the prior art may disclose using some of the same types of delivery devices as can be used with the claimed invention, that does not constitute a disclosure to actually do so. For example, a removable vaginal device such as referenced in US 6,328,991 in normal usage delivers drug to the vaginal canal, which is intended, but is not intended remove the delivered drug from the mucosal surface when the sponge is removed. To the contrary, all of the delivery devices in the cited art are intended conventionally to delivery the drug, but not then remove it. In order for the claimed invention to be practiced, the IRM compound needs to be put in contact with the mucosal surface but then at least 50% of it removed from the mucosal surface, for example by washing it off somehow or, preferably, by having it adhere more strongly to the delivery device than to the mucosal tissue. This is not the norm and merely removing a conventional device that may have residual drug compound in it does not constitute removing the drug that has been delivered to the mucosal surface. The present claims would not read on the devices as used according to the cited references because there is no reason to conclude that they are removing at least 50% of the IRM compound from the mucosal surface after application thereto.

In this regard, the '674 actually teaches away from the invention by (as noted in the Office Action) pointing out as a problem the potential for "wash away" of the IRM and also mentioning problems with irritation.

Accordingly, since none of the cited references in fact discloses or suggests subsequently removing at least 50% of the IRM from the mucosal surface, it is submitted that a prima facie case of obviousness has not been established. Moreover, it is further submitted that the present application and claimed invention clearly rebuts any prima facie case of obviousness in view of the unexpected result that the IRM compounds can quickly "jump-start" the immune response and the be removed from contact in order to reduce irritation effects of the IRM compound at the mucosal surface.

The rejection under 35 USC § 103(a) as being unpatentable over US 2002/0058674 in view of WO 99/29693 in further view of US patent 6,328,991 has been overcome and should be withdrawn.

In view of the above, it is submitted that the application is in condition for allowance.

Examination and reconsideration of the application as amended is requested.

Applicant requests a telephone interview to more fully understand the examiners position and advance this case to issuance.

Respectfully submitted,

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